

WHAT IS CLAIMED IS:

1. A composition-of-matter comprising a crystallized glucocerebrosidase molecule, wherein said crystallized glucocerebrosidase molecule is characterized by an X-ray diffraction capacity enabling generation of a set of structure coordinates defining a 3D structure of said glucocerebrosidase molecule or a portion thereof.
2. The composition-of-matter of claim 1, wherein said set of structure coordinates defines said 3D structure to a resolution of 2.9 angstroms or higher.
3. The composition-of-matter of claim 1, wherein an amino acid sequence of said glucocerebrosidase molecule is partially glycosylated.
4. The composition-of-matter of claim 1, wherein said crystallized glucocerebrosidase molecule is characterized by unit cell dimensions of $a =$ about 107.7 angstroms, $b =$ about 285.2 angstroms and $c =$ about 91.8 angstroms.
5. The composition-of-matter of claim 1, wherein said crystallized glucocerebrosidase molecule is characterized by a crystal space group of $C222_1$.
6. The composition-of-matter of claim 1, wherein said glucocerebrosidase molecule is capable of displaying normal enzymatic activity.
7. The composition-of-matter of claim 1, wherein an amino acid sequence of said glucocerebrosidase molecule is set forth in SEQ ID NO: 1.
8. The composition-of-matter of claim 1, wherein said set of structure coordinates comprises a set of structure coordinates set forth in Table 4, 5, 6, 7, 8, 9, and/or 10.
9. A method of identifying a compound capable of correcting an impaired enzymatic activity of a mutant glucocerebrosidase molecule, the method comprising:
 - (a) obtaining a first set of structure coordinates, said first set of structure

coordinates defining a 3D structure of a glucocerebrosidase molecule capable of displaying normal enzymatic activity or a portion thereof;

(b) computationally generating using said first set of structure coordinates a second set of structure coordinates, said second set of structure coordinates defining a predicted 3D structure of the mutant glucocerebrosidase molecule or a portion thereof; and

(c) computationally identifying, using said second set of structure coordinates, a compound capable of interacting with the mutant glucocerebrosidase molecule in such a way as to correct the impaired enzymatic activity thereof, thereby identifying the compound capable of correcting the impaired enzymatic activity of the mutant glucocerebrosidase molecule.

10. The method of claim 9, wherein step (c) is effected further using said first set of structure coordinates.

11. The method of claim 9, further comprising biochemically qualifying a capacity of the compound to correct the impaired enzymatic activity of the mutant glucocerebrosidase molecule.

12. The method of claim 9, wherein said first set of structure coordinates defines said 3D structure at a resolution of 2.9 angstroms or higher.

13. The method of claim 9, wherein an amino acid sequence of said glucocerebrosidase molecule capable of displaying normal enzymatic activity is partially glycosylated.

14. The method of claim 9, wherein an amino acid sequence of said glucocerebrosidase molecule capable of displaying normal enzymatic activity is set forth in SEQ ID NO: 1.

15. The method of claim 9, wherein an amino acid sequence of said glucocerebrosidase molecule capable of displaying normal enzymatic activity is

composed of 497 amino acid residues, and whereas said portion of said glucocerebrosidase molecule capable of displaying normal enzymatic activity comprises a set of amino acid residues of said amino acid sequence of said glucocerebrosidase molecule having normal activity having amino acid sequence coordinates selected from the group consisting of:

- (i) 76, 81, 285, 312, 314, 320, 324, 325, 336, 364–378, 423, and 433;
- (ii) 244–247, and 390–397;
- (iii) 20, 21, 95–100, and 404–411;
- (iv) 65–67, 440–447, 460–464, 468, and 469;
- (v) 360–366, 443–446, 460–467, and 484–89; and/or
- (vi) 33–35, 69, 71, 450–456, 474–478, and 493–497.

16. The method of claim 9, wherein an amino acid sequence of the mutant glucocerebrosidase molecule is composed of 497 amino acid residues, and whereas said portion of the mutant glucocerebrosidase molecule comprises a set of amino acid residues of said amino acid sequence of said mutant glucocerebrosidase molecule having amino acid sequence coordinates selected from the group consisting of:

- (i) 76, 81, 285, 312, 314, 320, 324, 325, 336, 364–378, 423, and 433;
- (ii) 244–247, and 390–397;
- (iii) 20, 21, 95–100, and 404–411;
- (iv) 65–67, 440–447, 460–464, 468, and 469;
- (v) 360–366, 443–446, 460–467, and 484–89; and/or
- (vi) 33–35, 69, 71, 450–456, 474–478, and 493–497.

17. The method of claim 9, wherein said first set of structure coordinates comprises a set of structure coordinates set forth in Table 4, 5, 6, 7, 8, 9, and/or 10.

18. The method of claim 9, wherein an amino acid sequence of the mutant glucocerebrosidase molecule is set forth in SEQ ID NO: 2, 3, 4, 5, 6, or 7.

19. The method of claim 9, wherein said second set of structure coordinates comprises a set of structure coordinates set forth in Table 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, and/or 22.

20. The method of claim 9, wherein said glucocerebrosidase molecule capable of displaying normal enzymatic activity is a crystallized glucocerebrosidase molecule.

21. The method of claim 20, wherein said crystallized glucocerebrosidase molecule is characterized by unit cell dimensions of a = about 107.7 angstroms, b = about 285.2 angstroms and c = about 91.8 angstroms.

22. The method of claim 20, wherein said crystallized glucocerebrosidase molecule is characterized by a crystal space group of C222₁.

23. A computing platform capable of generating a model representing a 3D structure of a glucocerebrosidase molecule or a portion thereof, the computing platform comprising:

- (a) a data-storage device storing data comprising a set of structure coordinates defining the 3D structure of the glucocerebrosidase molecule or the portion thereof; and
- (b) a processing unit being for generating the model representing the 3D structure from said data stored in said data-storage device.

24. The computing platform of claim 23, wherein said set of structure coordinates defines the 3D structure at a resolution of 2.9 angstroms or higher.

25. The computing platform of claim 23, wherein an amino acid sequence of the glucocerebrosidase molecule is partially glycosylated.

26. The computing platform of claim 23, wherein the glucocerebrosidase molecule is a glucocerebrosidase molecule capable of displaying normal enzymatic activity, or is a mutant glucocerebrosidase molecule.

27. The computing platform of claim 23, wherein an amino acid sequence of the glucocerebrosidase molecule is set forth in SEQ ID NO: 1, 2, 3, 4, 5, 6, or 7.

28. The computing platform of claim 23, wherein an amino acid sequence of the glucocerebrosidase molecule is composed of 497 amino acid residues, and whereas the portion of the glucocerebrosidase molecule comprises a set of amino acid residues of said amino acid sequence having amino acid sequence coordinates selected from the group consisting of:

- (i) 76, 81, 285, 312, 314, 320, 324, 325, 336, 364–378, 423, and 433;
- (ii) 244–247, and 390–397;
- (iii) 20, 21, 95–100, and 404–411;
- (iv) 65–67, 440–447, 460–464, 468, and 469;
- (v) 360–366, 443–446, 460–467, and 484–89; and/or
- (vi) 33–35, 69, 71, 450–456, 474–478, and 493–497.

29. The computing platform of claim 23, wherein said set of structure coordinates comprises a set of structure coordinates set forth in Table 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, and/or 22.

30. The computing platform of claim 23, wherein the glucocerebrosidase molecule is a crystallized glucocerebrosidase molecule.

31. The computing platform of claim 30, wherein said crystallized glucocerebrosidase molecule is characterized by unit cell dimensions of a = about 107.7 angstroms, b = about 285.2 angstroms and c = about 91.8 angstroms.

32. The computing platform of claim 30, wherein said crystallized glucocerebrosidase molecule is characterized by a crystal space group of $C222_1$.

33. A method of crystallizing a glucocerebrosidase molecule, the method comprising:

- (a) partially deglycosylating the glucocerebrosidase molecule, thereby generating a partially glycosylated glucocerebrosidase molecule; and
- (b) subjecting said partially glycosylated glucocerebrosidase molecule to crystallization-inducing conditions, thereby crystallizing the glucocerebrosidase molecule.

34. The method of claim 33, wherein step (a) is effected by treating the glucocerebrosidase molecule with N-glycosidase F.

35. The method of claim 33, wherein an amino acid sequence of the glucocerebrosidase molecule comprises a first N-linked glycosylation consensus sequence, wherein said first N-linked glycosylation consensus sequence is attached to a sugar moiety comprising a monosaccharide or a disaccharide directly attached to said first N-linked glycosylation consensus sequence, and whereas step (a) is effected so as to leave said monosaccharide or said disaccharide attached to said first N-linked glycosylation consensus sequence.

36. The method of claim 35, wherein said monosaccharide or disaccharide is composed of N-acetylglucosamine moieties.

37. The method of claim 35, wherein step (a) is further effected so as to fully deglycosylate all glycosylated N-linked glycosylation consensus sequences of said amino acid sequence of said glucocerebrosidase molecule other than said first N-linked glycosylation consensus sequence of said amino acid sequence of said glucocerebrosidase molecule.

38. The method of claim 33, wherein said crystallization-inducing conditions comprise inducing evaporation of a crystallization solution containing said at least partially deglycosylated glucocerebrosidase molecule at a concentration of about 5 mg/ml, and a component selected from the group consisting of a buffer, a sodium salt, an ammonium salt, a sulfate salt, a chaotropic compound, a potassium salt, and a chloride ion.

39. The method of claim 38, wherein said buffer is a Zwitterionic buffer or an acetate buffer.

40. The method of claim 38, wherein said buffer is 2-morpholinoethanesulfonic acid buffer or sodium acetate buffer.

41. The method of claim 38, wherein said crystallization solution contains said buffer at a concentration of about 0.5 millimolar or about 0.05 molar.

42. The method of claim 38, wherein said solution of a buffer has a pH of about 6.6 or about 4.6.

43. The method of claim 38, wherein said sodium salt is sodium chloride.

44. The method of claim 38, wherein said crystallization solution contains said sodium salt at a concentration of about 0.05 molar.

45. The method of claim 38, wherein said ammonium salt is ammonium sulfate.

46. The method of claim 38, wherein said crystallization solution contains said ammonium salt at a concentration of about 0.5 molar.

47. The method of claim 38, wherein said crystallization solution contains said sulfate salt at a concentration of about 0.5 molar.

48. The method of claim 38, wherein said chaotropic compound is guanidine hydrochloride.

49. The method of claim 38, wherein said crystallization solution contains said chaotropic compound at a concentration of about 0.085 molar.

50. The method of claim 38, wherein said potassium salt is potassium chloride.

51. The method of claim 38, wherein said crystallization solution contains said potassium salt at a concentration of about 0.01 molar.

52. The method of claim 38, wherein said crystallization solution contains

said chloride ion at a concentration of about 0.06 molar.

53. The method of claim 38, wherein said crystallization solution has a pH of about 4.6.

54. The method of claim 38, wherein said inducing evaporation of said crystallization solution is effected at a temperature of about 22 degrees centigrade.

55. A computer-readable medium comprising, in a retrievable format, data including a set of structure coordinates defining a 3D structure of a glucocerebrosidase molecule or a portion thereof, wherein said set of structure coordinates defines said 3D structure at a resolution of 2.9 angstroms or higher, and/or wherein an amino acid sequence of said glucocerebrosidase molecule is partially glycosylated.

56. A computer generated model representing a 3D structure of a glucocerebrosidase molecule or a portion thereof, wherein the model represents said glucocerebrosidase molecule or a portion thereof at a resolution of 2.9 angstroms or higher, and/or wherein an amino acid sequence of said glucocerebrosidase molecule is partially glycosylated.

57. A glucocerebrosidase preparation comprising a population of glucocerebrosidase molecules, wherein substantially each of said glucocerebrosidase molecules:

- (i) has an amino acid sequence at least 95 percent homologous to an amino acid sequence set forth by SEQ ID NO: 1 or 8;
- (ii) is glycosylated at, or has an aspartic acid residue at, glycosylation residue 1 of said amino acid sequence; and
- (iii) is independently unglycosylated at one or more glycosylation residues selected from the group consisting of glycosylation residues 2, 3 and 4 of said amino acid sequence.

58. The glucocerebrosidase preparation of claim 57, wherein said

glycosylation residue 1 is represented by Asn19 of SEQ ID NO: 1, 8 or 16.

59. The glucocerebrosidase preparation of claim 57, wherein said glycosylation residue 2 is represented by Asn59 of SEQ ID NO: 1, 8 or 16.

60. The glucocerebrosidase preparation of claim 57, wherein said glycosylation residue 3 is represented by Asn146 of SEQ ID NO: 1, 8 or 16.

61. The glucocerebrosidase preparation of claim 57, wherein said glycosylation residue 4 is represented by Asn270 of SEQ ID NO: 1, 8 or 16.

62. The glucocerebrosidase preparation of claim 57, wherein said population of glucocerebrosidase molecules, following an incubation in phosphate-buffered saline solution at a temperature of 25 degrees centigrade for a duration of at least 40 hours, has about the same capacity to catalyze hydrolysis of a glucocerebroside as a population of fully glycosylated glucocerebrosidase molecules each having an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or 8.

63. The glucocerebrosidase preparation of claim 57, wherein said population of glucocerebrosidase molecules has about the same capacity to catalyze hydrolysis of a glucocerebroside as a population of fully glycosylated glucocerebrosidase molecules having an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or 8.

64. The glucocerebrosidase preparation of claim 57, wherein at least one glycosylation moiety of each of at least some of said glucocerebrosidase molecules has at least one exposed mannose residue.

65. The glucocerebrosidase preparation of claim 57, wherein at least some of said glucocerebrosidase molecules are capable of being internalized by a phagocyte.

66. A pharmaceutical composition for treating a disease associated with glucocerebrosidase deficiency in a subject in need thereof, the pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as an active ingredient, a glucocerebrosidase preparation comprising a population of glucocerebrosidase molecules, wherein substantially each of said glucocerebrosidase molecules:

- (i) has an amino acid sequence at least 95 percent homologous to an amino acid sequence set forth by SEQ ID NO: 1 or 8;
- (ii) is glycosylated at, or has an aspartic acid residue at, glycosylation residue 1 of said amino acid sequence; and
- (iii) is independently unglycosylated at one or more glycosylation residues selected from the group consisting of glycosylation residues 2, 3 and 4 of said amino acid sequence.

67. The pharmaceutical composition of claim 66, wherein said pharmaceutically acceptable carrier is selected so as to enable administration of the pharmaceutical composition via a route selected from the group consisting of the intravenous, topical, intranasal, transdermal, intradermal, oral, buccal, parenteral, rectal and inhalation route.

68. The pharmaceutical composition of claim 66, wherein said glycosylation residue 1 is represented by Asn19 of SEQ ID NO: 1, 8 or 16.

69. The pharmaceutical composition of claim 66, wherein said glycosylation residue 2 is represented by Asn59 of SEQ ID NO: 1, 8 or 16.

70. The pharmaceutical composition of claim 66, wherein said glycosylation residue 3 is represented by Asn146 of SEQ ID NO: 1, 8 or 16.

71. The pharmaceutical composition of claim 66, wherein said glycosylation residue 4 is represented by Asn270 of SEQ ID NO: 1, 8 or 16.

72. The pharmaceutical composition of claim 66, wherein said population

of glucocerebrosidase molecules, following an incubation in phosphate-buffered saline solution at a temperature of 25 degrees centigrade for a duration of at least 40 hours, has about the same capacity to catalyze hydrolysis of a glucocerebroside as a population of fully glycosylated glucocerebrosidase molecules each having an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or 8.

73. The pharmaceutical composition of claim 66, wherein said population of glucocerebrosidase molecules has about the same capacity to catalyze hydrolysis of a glucocerebroside as a population of fully glycosylated glucocerebrosidase molecules having an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or 8.

74. The pharmaceutical composition of claim 66, wherein at least one glycosylation moiety of each of at least some of said glucocerebrosidase molecules has at least one exposed mannose residue.

75. The pharmaceutical composition of claim 66, wherein at least some of said glucocerebrosidase molecules are capable of being internalized by a phagocyte.

76. A method of producing a glucocerebrosidase preparation suitable for treatment of a disease associated with glucocerebrosidase deficiency, the method comprising exposing a plurality of glucocerebrosidase molecules to conditions suitable for partial deglycosylation thereof so as to form a population of partially deglycosylated glucocerebrosidase molecules each characterized by an amino acid sequence:

- (i) glycosylated at, or having an aspartic acid residue at, glycosylation residue 1 thereof; and
- (ii) lacking glycosylation at one or more glycosylation residues thereof selected from the group consisting of glycosylation residues 2, 3 and 4, thereby producing a glucocerebrosidase preparation suitable for treatment of a disease associated with glucocerebrosidase deficiency.

77. The method of claim 76, further comprising, prior to and/or

concomitantly with said exposing said plurality of glucocerebrosidase molecules to said conditions, subjecting said plurality of glucocerebrosidase molecules to conditions suitable for exposing at least one mannose residue of at least one glycosylation moiety of each of at least some of said glucocerebrosidase molecules of said plurality of glucocerebrosidase molecules.

78. The method of claim 76, further comprising subjecting said population of partially deglycosylated glucocerebrosidase molecules to conditions suitable for exposing at least one mannose residue of at least one glycosylation moiety of each at least some of said partially glycosylated glucocerebrosidase molecules.

79. The method of claim 76, wherein said conditions suitable for partial deglycosylation of said glucocerebrosidase molecules include treating said plurality of glucocerebrosidase molecules with a glycosidase.

80. The method of claim 76, wherein said conditions suitable for partial deglycosylation of said glucocerebrosidase molecules include treating said plurality of glucocerebrosidase molecules with peptide N-glycosidase F.

81. The method of claim 76, wherein said amino acid sequence is at least 95 percent homologous to an amino acid sequence set forth by SEQ ID NO: 1 or 8;

82. The method of claim 81, wherein said glycosylation residue 1 is represented by Asn19 of SEQ ID NO: 1, 8 or 16.

83. The method of claim 81, wherein said glycosylation residue 2 is represented by Asn59 of SEQ ID NO: 1, 8 or 16.

84. The method of claim 81, wherein said glycosylation residue 3 is represented by Asn146 of SEQ ID NO: 1, 8 or 16.

85. The method of claim 81, wherein said glycosylation residue 4 is represented by Asn270 of SEQ ID NO: 1, 8 or 16.

86. The method of claim 76, wherein the disease associated with glucocerebrosidase deficiency is Gaucher disease.

87. An article of manufacture comprising packaging material and a pharmaceutical composition, the article of manufacture being identified for treatment of a disease associated with glucocerebrosidase deficiency in a subject in need thereof; the pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as an active ingredient, a glucocerebrosidase preparation comprising a population of glucocerebrosidase molecules, wherein substantially each of said glucocerebrosidase molecules:

- (i) has an amino acid sequence at least 95 percent homologous to an amino acid sequence set forth by SEQ ID NO: 1 or 8;
- (ii) is glycosylated at, or has an aspartic acid residue at, glycosylation residue 1 of said amino acid sequence; and
- (iii) is independently unglycosylated at one or more glycosylation residues selected from the group consisting of glycosylation residues 2, 3 and 4 of said amino acid sequence.

88. The article of manufacture of claim 87, wherein said glycosylation residue 1 is represented by Asn19 of SEQ ID NO: 1, 8 or 16.

89. The article of manufacture of claim 87, wherein said glycosylation residue 2 is represented by Asn59 of SEQ ID NO: 1, 8 or 16.

90. The article of manufacture of claim 87, wherein said glycosylation residue 3 is represented by Asn146 of SEQ ID NO: 1, 8 or 16.

91. The article of manufacture of claim 87, wherein said glycosylation residue 4 is represented by Asn270 of SEQ ID NO: 1, 8 or 16.

92. The article of manufacture of claim 87, wherein said population of glucocerebrosidase molecules, following an incubation in phosphate-buffered saline solution at a temperature of 25 degrees centigrade for a duration of at least 40 hours,

has about the same capacity to catalyze hydrolysis of a glucocerebroside as a population of fully glycosylated glucocerebrosidase molecules each having an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or 8.

93. The article of manufacture of claim 87, wherein said population of glucocerebrosidase molecules has about the same capacity to catalyze hydrolysis of a glucocerebroside as a population of fully glycosylated glucocerebrosidase molecules having an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or 8.

94. The article of manufacture of claim 93, wherein said population of glucocerebrosidase molecules has said about the same capacity to catalyze hydrolysis of a glucocerebroside following an incubation in phosphate-buffered saline solution at a temperature of 25 degrees centigrade for a duration of at least 40 hours.

95. The article of manufacture of claim 87, wherein at least one glycosylation moiety of each of at least some of said glucocerebrosidase molecules has at least one exposed mannose residue.

96. The article of manufacture of claim 87, wherein at least some of said glucocerebrosidase molecules are capable of being internalized by a phagocyte.

97. The article of manufacture of claim 87, wherein said disease associated with glucocerebrosidase deficiency is Gaucher disease.

98. A method of increasing glucocerebrosidase activity in a cell, the method comprising exposing the cell to a glucocerebrosidase preparation comprising a population of glucocerebrosidase molecules, wherein substantially each of said glucocerebrosidase molecules:

- (i) has an amino acid sequence at least 95 percent homologous to an amino acid sequence set forth by SEQ ID NO: 1 or 8;
- (ii) is glycosylated at, or has an aspartic acid residue at, glycosylation residue 1 of said amino acid sequence; and

(iii) is independently unglycosylated at one or more glycosylation residues selected from the group consisting of glycosylation residues 2, 3 and 4 of said amino acid sequence,

thereby inducing substantial glucocerebrosidase activity in a cell.

99. The method of claim 98, wherein said exposing the cell to said glucocerebrosidase preparation is effected by administering said glucocerebrosidase preparation to a subject.

100. The method of claim 98, wherein said exposing the cell to said glucocerebrosidase preparation is effected *in-vitro*.

101. The method of claim 98, wherein said glycosylation residue 1 is represented by Asn19 of SEQ ID NO: 1, 8 or 16.

102. The method of claim 98, wherein said glycosylation residue 2 is represented by Asn59 of SEQ ID NO: 1, 8 or 16.

103. The method of claim 98, wherein said glycosylation residue 3 is represented by Asn146 of SEQ ID NO: 1, 8 or 16.

104. The method of claim 98, wherein said glycosylation residue 4 is represented by Asn270 of SEQ ID NO: 1, 8 or 16.

105. The method of claim 98, wherein said population of glucocerebrosidase molecules, following an incubation in phosphate-buffered saline solution at a temperature of 25 degrees centigrade for a duration of at least 40 hours, has about the same capacity to catalyze hydrolysis of a glucocerebroside as a population of fully glycosylated glucocerebrosidase molecules each having an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or 8.

106. The method of claim 98, wherein said population of glucocerebrosidase molecules has about the same capacity to catalyze hydrolysis of a glucocerebroside as

a population of fully glycosylated glucocerebrosidase molecules having an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or 8.

107. The method of claim 98, wherein at least one glycosylation moiety of each of at least some of said glucocerebrosidase molecules has at least one exposed mannose residue.

108. The method of claim 98, wherein at least some of said glucocerebrosidase molecules are capable of being internalized by a phagocyte.

109. The method of claim 98, wherein the cell is a phagocyte.

110. A method of treating a disease associated with glucocerebrosidase deficiency in a subject in need thereof, the method comprising administering to the subject in need thereof a therapeutically effective amount of a glucocerebrosidase preparation comprising a population of glucocerebrosidase molecules, wherein substantially each of said glucocerebrosidase molecules:

- (i) has an amino acid sequence at least 95 percent homologous to an amino acid sequence set forth by SEQ ID NO: 1 or 8;
- (ii) is glycosylated at, or has an aspartic acid residue at, glycosylation residue 1 of said amino acid sequence; and
- (iii) is independently unglycosylated at one or more glycosylation residues selected from the group consisting of glycosylation residues 2, 3 and 4 of said amino acid sequence,

thereby treating a disease associated with glucocerebrosidase deficiency in a subject in need thereof.

111. The method of claim 110, wherein said administering to the subject in need thereof a therapeutically effective amount of a glucocerebrosidase preparation is effected via systemic administration.

112. The method of claim 110, wherein said administering to the subject in need thereof a therapeutically effective amount of a glucocerebrosidase preparation is

effected via local administration.

113. The method of claim 110, wherein said glycosylation residue 1 is represented by Asn19 of SEQ ID NO: 1, 8 or 16.

114. The method of claim 110, wherein said glycosylation residue 2 is represented by Asn59 of SEQ ID NO: 1, 8 or 16.

115. The method of claim 110, wherein said glycosylation residue 3 is represented by Asn146 of SEQ ID NO: 1, 8 or 16.

116. The method of claim 110, wherein said glycosylation residue 4 is represented by Asn270 of SEQ ID NO: 1, 8 or 16.

117. The method of claim 110, wherein said population of glucocerebrosidase molecules, following an incubation in phosphate-buffered saline solution at a temperature of 25 degrees centigrade for a duration of at least 40 hours, has about the same capacity to catalyze hydrolysis of a glucocerebroside as a population of fully glycosylated glucocerebrosidase molecules each having an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or 8.

118. The method of claim 110, wherein said population of glucocerebrosidase molecules has about the same capacity to catalyze hydrolysis of a glucocerebroside as a population of fully glycosylated glucocerebrosidase molecules having an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or 8.

119. The article of manufacture of claim 118, wherein said population of glucocerebrosidase molecules has said about the same capacity to catalyze hydrolysis of a glucocerebroside following an incubation in phosphate-buffered saline solution at a temperature of 25 degrees centigrade for a duration of at least 40 hours.

120. The method of claim 110, wherein at least one glycosylation moiety of

each of at least some of said glucocerebrosidase molecules has at least one exposed mannose residue.

121. The method of claim 110, wherein at least some of said glucocerebrosidase molecules are capable of being internalized by a phagocyte.

122. The method of claim 110, wherein the disease associated with glucocerebrosidase deficiency is Gaucher disease.